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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,836	06/12/2001	Laurent F A Hennequin	P.278065	6411
9629	7590	02/10/2005	EXAMINER	
MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004			TRUONG, TAMTHOM NGO	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

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<b>Office Action Summary</b>	<b>Application No.</b> 09/806,836	<b>Applicant(s)</b> HENNEQUIN ET AL.	
	<b>Examiner</b> Tamthom N. Truong	<b>Art Unit</b> 1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 November 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 5-14 and 16-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10-13 is/are allowed.
- 6) ☒ Claim(s) 5-9, 14 and 16-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Applicant's amendment, argument and declaration of 11-19-04 have been fully considered. However, applicant's argument regarding the term "thiophenoxy" in US'969 cited in the previous 103 rejection has not found persuasive. Also, the declaration under 37 CFR 1.132 filed 11-19-04 is insufficient to overcome the rejection of claims 5-9, 14 and 16-19 based upon **Myers et. al.** (US 6,645,969 B1) as set forth in the last Office action because compounds C1 and C2 in the declaration are not the compounds relied upon for the previous 103 rejection. Therefore, the previous 103 rejection is maintained herein.
2. There are a few 112/2<sup>nd</sup> issues noted, and thus prompting a new ground of rejection. Also, a newly found reference raises another 103 rejection.
3. Examiner Truong wishes to apologize for the indication of "two references" when only one was applied in the previous office action.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 5-9, 13, 14, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Myers et. al.** (US 6,645,969 B1) in view of ***Hawley's Condensed Chemical Dictionary***.

As mentioned in the previous office action, Myers et. al. list several compounds of which two compounds on lines 54 and 58 are analogous to those of formula (II) in the instant claims 5-9, 14 and 18 with the following substituents:

$Z_b$  is -O-; and ring C is a 5-membered heterocyclic moiety (e.g., thiophene);

$R^{2a}$  is alkoxy.

The disclosed compounds differ from the claimed compounds by having a halogen or methoxy as a substituent corresponding to the instant variable  $R^2$  (which has been excluded from claim 18).

However, on column 3 of US'969, the disclosed genus of formula I provides equivalent teaching for many substituents on the quinazoline such as: alkylthio, hydroxy, carboxy, and carbalkoxy, etc. (see definition of  $R_7$  which corresponds to the instant variable  $R^2$ ). Also, the disclosed variable R (corresponding to the instant variable  $R^1$ ) represents moieties that overlap with those represented by the instant variable  $R^1$  (e.g. hydrogen, alkyl, aryl, aralkyl, etc.). With such an equivalent teaching, one skilled in the art would have been motivated to select the claimed compounds since the general process for making said compounds is also described on columns 5 and 6 (which is analogous to the process (a) recited in the instant claim 19).

Applicant argued that the cited compounds:

*4-(3-methoxythiophenoxy)-6,7-dimethoxyquinazoline*, and

*4-(3-chlorothiophenoxy)-6,7-dimethoxyquinazoline*,

did not have the ring “thiophene” connected to –O– as suggested by the term “*thiophenoxy*”. Applicant asserted that the term “*thiophenoxy*” actually means “thiophenyl” (i.e., phenyl-S-). However, *Hawley’s Condensed Chemical Dictionary* defines the term “thiophenol” as “phenyl-mercaptan” (or phenyl-SH), and does not list a definition for “*thiophenoxy*” as thiophenyl as suggested by applicant. Besides, applicant did not provide any reference to support his interpretation. Furthermore, on column 3, Myers et. al. list the preferred groups for Ar (corresponding to the instant ring C) which includes “benzene, pyrrole, **thiophene**, furan, thiazole, imidazole, etc.)—see column 3, lines 40-45. Thus, it would be reasonable to interpret “*thiophenoxy*” to mean ‘thiophene-O-’ unless proven otherwise.

Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Myers et. al.** (US’969) in view of **Mohammadi et. al.** (The EMBO Journal, 1998, Vol. 17, No. 20, pp. 5896-5904).

Applicant asserted method claims 16 and 17 are distinguished from the teaching of Myers et. al. since there is no explicit disclosure of angiogenesis and/or vascular permeability in the teaching of Myers et. al. Applicant further explained that “an implicit or inherent disclosure, *one that is unspoken, cannot* support an obviousness rejection.” To rectify the inherency in Myers et. al., the teaching of **Mohammadi et. al.** is now cited.

The compounds of Myers et. al. inhibit cellular proliferation to treat disorders such as “cancer, leukemia, psoriasis, inflammatory diseases, bone diseases, **atherosclerosis** and *restenosis...*” While Myers et. al. do not relate atherosclerosis to angiogenesis, Mohammadi et. al. disclose that “*Pathological angiogenesis is a feature of various disease conditions such as*

*diabetic retinopathy, atherosclerosis and psoriasis.*” – see the first paragraph of the “Introduction”, page 5896, right column, lines 8-10. Therefore, it would have been obvious for one skilled in the art to use the compounds of Myers et. al. in the treatment of angiogenesis and vascular permeability because said compounds could inhibit the growth of endothelial cells inside the vessels which ultimately inhibit angiogenesis and vascular permeability.

5. Claims 5-9 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Manning et. al.** (WO 87/04321). On page 117, Table 14 discloses a triazolyl compound substituted with a quinazolin-oxy. Said compound is analogous to the compound of the instant formula II with following substituent:

$Z_b$  is  $-O-$ ;

Ring C is a 6-membered heteroaryl group (e.g., triazinyl).

The disclosed compound differs from the instant formula II by having a substituent at the 8<sup>th</sup> position, and not 7<sup>th</sup> position on the quinazoline ring. Also, the disclosed compound differs from the instant formula II by having a substituent of  $CH_3SO_2$  on the triazinyl ring which is not a moiety represented by the instant variable  $R^1$ . However, on columns 5-13, the reference discloses a generic formula 1 of  $R_1-X-R_2$ , in which both  $R_1$  and  $R_2$  can be a heteroaryl group substituted with a substituent Z that can be **anywhere on the ring** (e.g., see pages 25 and 30). The substituent Z can be any moiety listed on page 13 which includes *hydroxy, cyano, nitro, trifluoromethyl*, etc. Thus, the generic disclosure provides equivalent teaching for many moieties as a substituent on ring  $R_1$  or  $R_2$ , as well as for all the positions on both rings.

Such a disclosure would have motivated one skilled in the art to select compounds of formula II with ring C as triazine, and Z<sub>b</sub> as -O- because one would have expected said compounds to reduce the transpirational moisture loss from plants as well.

Therefore, at the time of the invention, it would have been obvious to make some compounds of formula II in view of the teaching of Manning et. al.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 5-9, 14 and 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. Claim 18 recites many limitations within parenthesis which is unclear if said limitations are part of the claim.
- b. Claims 5-9, 14, and 16-19 are rejected as being dependent on claim 18 as well.
- c. Claim 9 lacks antecedent basis because it recites "halogen" for R<sup>2</sup>, which is not recited in claim 18—a claim it depends on.

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*Allowable Subject Matter*

7. Claims 10-12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Claim 13 is allowable.

The following is a statement of reasons for the indication of allowable subject matter:

Claims 10-13 recite quinazoline species that are substituted with specific  $R^2$  and  $Z_b$ -ring  $C-R_1$  groups that are not taught in the prior arts of record. The compounds with the specific combination of substituents as recited in claims 10-13 are simply not disclosed or fairly suggested by Myers et. al. or Manning et. al.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

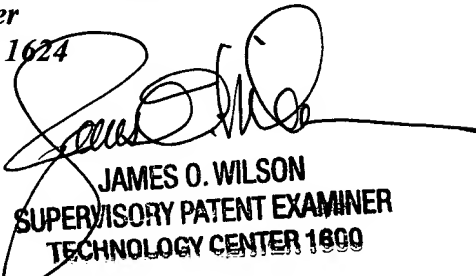
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*Tamthom N. Truong*  
Examiner  
Art Unit 1624

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02-03-05

  
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